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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
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EXAMINER	
KETTER, JAMES S	

ART UNIT	PAPER NUMBER
1636	

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Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/532,197	PRENTICE, HOLLY	
	Examiner	Art Unit	
	James S. Ketter	1636	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *01 August 2008*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *22-49,51-68 and 70* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☒ Claim(s) *63 and 64* is/are allowed.

6)☒ Claim(s) *22-49,51-53,55-62,65-68 and 70* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *21 April 2005* is/are: a)☒ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *11/18/08*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

The newly discovered reference to Ai et al. (see all rejections below) has led to the new grounds of rejection, below. The delay in presenting this reference is regretted.

To the extent that Applicant's arguments presented in the amendment filed 1 August 2008 apply to the newly presented rejections, they will be addressed. Arguments regarding the lack of a teaching in Perkins et al. of the specific 3' regulatory region as now present in all claims, is believed addressed by the inclusion of this reference to Ai et al.

Claims 63 and 64 are allowed.

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

Claims 22-30, 33, 35-38, 41-43, 50-53, 55-62, 65-68 and 70 are rejected under 35 U.S.C. 103(a) as being unpatentable over Perkins et al. (of record) in view of Ai et al. (U, newly cited).

The instant claims were described in the Office Action mailed 2 April 2008, except that they are all now limited to the proximal 3' regulatory sequences comprising a sequence of at least 100 bases having at least 70% identity to a nucleotide sequence found within the proximal 3' regulatory sequences of a ferritin heavy chain gene locus.

Perkins et al. was described in the Office Action mailed 2 April 2008. Perkins et al. differs from the claimed invention in not teaching that the 3' region comprises a sequence of at

least 100 bases having at least 70% identity to a nucleotide sequence found within the proximal 3' regulatory sequences of a ferritin heavy chain gene. Ai et al. teaches, e.g., as summarized in the Abstract, insertion of the 3' untranslated region of the ferritin heavy chain gene at the end of a different gene, in this case the luciferase gene. It is taught that this destabilized the luciferase trnacript unless PMA were added. Thus, the luciferase gene became PMA-regulated.

It would have been obvious to one of ordinary skill in the art to have substituted the ferritin heavy chain gene 3' untranslated region taught by Ai et al. for the SV40 3' region used in the construct taught by Perkins et al. The substitution of one known element (Ferritin heavy chain 3' region shown in Ai et al.) for another (SV40 3' region shown in Perkins et al.) would have been obvious to one of ordinary skill in the art at the time of the invention since the substitution of the ferritin 3' region would have yielded predictable results, namely regulation of stability of the transcript expressed by the Perkins et al. construct, and therefore of the gene thus encoded, by addition of PMA.

Claims 22, 34, 39, 40, 44 and 45 are rejected under 35 U.S.C. 103(a) as being unpatentable over Perkins et al. (of record) in view of Kwak et al. (of record) and Ai et al. (U, newly cited).

The instant claims were described in the Office Action mailed 2 April 2008, except that they are all now limited to the proximal 3' regulatory sequences comprising a sequence of at least 100 bases having at least 70% identity to a nucleotide sequence found within the proximal 3' regulatory sequences of a ferritin heavy chain gene locus, and the 5' flanking regions in the vector can comprise ferritin heavy chain locus 5' sequences with a total length of between 1,000

and 10,000 bases or at least 500 nucleotides found between 1 bp or between 20 bp up to 10,000 bp from the translation initiation codon of a ferritin heavy chain locus or at least 70% identity to said sequences.

Perkins et al. and Kwak et al. were described in the Office Action mailed 2 April 2008. Ai et al. is described above. Perkins et al. differs from the claimed invention in not teaching that the 3' region comprises a sequence of at least 100 bases having at least 70% identity to a nucleotide sequence found within the proximal 3' regulatory sequences of a ferritin heavy chain gene, and also in not teaching that ferritin heavy chain locus 5' sequences with a total length of between 1,000 and 10,000 bases or at least 500 nucleotides found between 1 bp or between 20 bp up to 10,000 bp from the translation initiation codon of a ferritin heavy chain locus or at least 70% identity to said sequences.

It would have been obvious to one of ordinary skill in the art to have included sequences at least 500 bases or between 1,000 to several thousand bases from the ferritin heavy chain gene promoter because Perkins et al. teaches that a ferritin heavy chain gene promoter can be used in recombinant expression vectors and because Kwak et al. teaches important additional promoter elements located in regions up to several kb 5' from the transcriptional start site of the ferritin heavy chain gene, and further to have substituted the ferritin heavy chain gene 3' untranslated region taught by Ai et al. for the SV40 3' region used in the construct taught by Perkins et al. The substitution of one known element (the regulatory elements shown in Kwak et al. for the regulatory elements shown in the vector of Perkins et al.) and (the ferritin heavy chain 3' region shown in Ai et al.) for another (SV40 3' region shown in Perkins et al.) would have been obvious to one of ordinary skill in the art at the time of the invention since the substitution of the ferritin

5' regulatory region would have yielded predictable results, namely the expression of the gene cloned in the vector, and substitution of the ferritin 3' region would have yielded predictable results, namely regulation of stability of the transcript expressed by the Perkins et al. construct, and therefore of the gene thus encoded, by addition of PMA.

At page 25 of the amendment filed 1 August 2008, Applicant argues that the position of the regulatory sequences in Kwak et al. would not have led predictably to basal level expression from the ferritin heavy gene promoter. However, it does not appear that this is a limitation in the instant claims.

Claims 22 and 46-49 are rejected under 35 U.S.C. 103(a) as being unpatentable over Perkins et al. (of record) in view either of Eglitis et al. (of record) or Hillgenberg et al. (if record), and Ai et al. (U, newly cited).

The instant claims were described in the Office Action mailed 2 April 2008, except that they are all now limited to the proximal 3' regulatory sequences comprising a sequence of at least 100 bases having at least 70% identity to a nucleotide sequence found within the proximal 3' regulatory sequences of a ferritin heavy chain gene locus, and that the insertion site is 0, 1, 2, 3, 4 or 1000 or 5,000 bp in length.

Perkins et al., Eglitis et al. and Hillgenberg et al. are described in the office Action mailed 2 April 2008. Ai et al. is described above. Perkins et al differs from the claimed invention innot teaching the particular sizes of the insertion site, and in not teaching that the 3' region comprises a sequence of at least 100 bases having at least 70% identity to a nucleotide sequence found within the proximal 3' regulatory sequences of a ferritin heavy chain gene.

It would have been obvious to one of ordinary skill in the art to have substituted the ferritin heavy chain gene 3' untranslated region taught by Ai et al. for the SV40 3' region used in the construct taught by Perkins et al., and to have included insertion sites of the claimed type in the vectors described by Perkins et al. because insertion sites for insertion of heterologous sequences of interest into vectors are standard in the construction of expression vectors and any sequence (of any size) can be an insertion site in the vector as long as it contains a sequence which can be cleaved by a restriction endonuclease, as shown by see Eglitis et al. or Hillgenberg et al. Applicant claims vectors with insertion sites of various sizes. Perkins et al. teaches the claimed vectors with multiple cloning sites which contain multiple restriction endonuclease cleavage sites. Each cleavage site can be considered an insertion site and a given multiple cleavage site can contain sites for blunt end restriction enzymes or sequences of 1 or 2 or 3 or 4 bases which can be sites of endonuclease cleavage or the insertion site can be any length of DNA with suitable restriction endonuclease cleavage sites, as noted by Hillgenberg et al. Essentially all expression vectors have sites for insertion of foreign nucleic acid sequences as the vectors are designed to accommodate foreign sequences for expression in host cells. One of ordinary skill in the art would have been motivated to include insertion sites of the type recited in the claims in the vectors described by Perkins et al. because Eglitis et al. or Hillgenberg et al. teach that any insertion sites can be engineered into vectors in terms of multiple cloning sites or that any sequence of any size can comprise an insertion site as long as it comprises a restriction endonuclease cleavage site. The specific claimed sizes of insertion sites (i.e. 0, 1, 2, 4, 1,000, 5,000 bp) must be considered a matter of design choice since sequences of any size can comprise an insertion site for heterologous nucleic acids of interest. Furthermore, the substitution of one

known element (Ferritin heavy chain 3' region shown in Ai et al.) for another (SV40 3' region shown in Perkins et al.) would have been obvious to one of ordinary skill in the art at the time of the invention since the substitution of the ferritin 3' region would have yielded predictable results, namely regulation of stability of the transcript expressed by the Perkins et al. construct, and therefore of the gene thus encoded, by addition of PMA.

At page 28, Applicant argues that the lengths of the insertion site are not described or suggested by the references. However, as set forth in the rejection, one of ordinary skill in the art would have expected any length of insertion site to operate in the art-known manner, the length being an arbitrary design choice. There is nothing unexpected about the insertion site lengths recited by Applicant.

Claims 31 and 32 are rejected under 35 U.S.C. 103(a) as being unpatentable over Perkins et al. (of record) in view of German et al. (of record) or Huston et al. (of record), and Ai et al. (U, newly cited).

The instant claims were described in the Office Action mailed 2 April 2008, except that they are all now limited to the proximal 3' regulatory sequences comprising a sequence of at least 100 bases having at least 70% identity to a nucleotide sequence found within the proximal 3' regulatory sequences of a ferritin heavy chain gene locus, and the proximal 5' regulatory sequences of the vector include a eukaryotic intron sequence or an intron sequence derived from intron 1 of a ferritin heavy chain gene..

Perkins et al., German et al. and Huston et al. were described in the Office Action mailed 2 April 2008. Perkins et al. differs from the claimed invention in not teaching that the 3' region

comprises a sequence of at least 100 bases having at least 70% identity to a nucleotide sequence found within the proximal 3' regulatory sequences of a ferritin heavy chain gene and in not teaching the use of intron sequences in the 5' regulatory region of the vector. Ai et al. is described above.

It would have been obvious to one of ordinary skill in the art to have included intron sequences into the 5' regulatory region of the vector because inclusion of intron sequences in 5' regulatory regions of expression vectors had been a standard technique known in the art, as shown in either German et al. or Huston et al., wherein the intron sequences served to enhance expression of the heterologous gene of interest. The motivation for inclusion of intron sequences into promoter regions in expression vectors so as to enhance expression thus would have come from either German et al. or Huston et al. Furthermore, it would have been obvious to one of ordinary skill to have substituted the ferritin heavy chain gene 3' untranslated region taught by Ai et al. for the SV40 3' region used in the construct taught by Perkins et al. The substitution of one known element (Ferritin heavy chain 3' region shown in Ai et al.) for another (SV40 3' region shown in Perkins et al.) would have been obvious to one of ordinary skill in the art at the time of the invention since the substitution of the ferritin 3' region would have yielded predictable results, namely regulation of stability of the transcript expressed by the Perkins et al. construct, and therefore of the gene thus encoded, by addition of PMA.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to James S. Ketter whose telephone number is 571-272-0770. The examiner can normally be reached on Monday-Friday.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Christopher Low can be reached on 571-272-0951. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

JSK
29 June 2009

/James S. Ketter/
Primary Examiner, Art Unit 1636